Sentara Health Plans Clinical Practice Guideline:

Perinatal and Postpartum Depression

Guideline History

Date Approved	9/04
Date Revised	7/06, 3/08, 1/10. 3/12, 3/14, 3/16, 3/18, 3/20, 3/22, 3/24, 3/26
Date Reviewed	3/26
Next Review Date	3/28

Key Points

General:

✓ Discuss risks, benefits and alternatives. Document this discussion and the patient's consent to the treatment plan.

Depression:

- ✓ Depression is very common in women, especially in women of reproductive age. It is estimated that 14%-23% of pregnant women experience depression during pregnancy, and 5%-25% experience depression postpartum.
- ✓ Perinatal depression affects as many as one in seven women. The American College of Obstetricians and Gynecologists recommends all pregnant women be screened at least once during the perinatal period.
- ✓ SSRIs are allowed. to be continued. and./or initiated. during pregnancy.
- ✓ Significant risk factors for perinatal depression include personal or family history of depression; discontinuation of antidepressant prior to or during pregnancy; poor social support; marital or relationship problems; ambivalence about the pregnancy.
- ✓ The Edinburgh Postnatal Depression Scale (EPDS) has been 100% sensitive and 95.5% specific in detecting major postpartum depression at a threshold score higher than 13. Use of a formal screening tool significantly increases the detection rate of antenatal depression. EPDS is being administered in the hospital, at the postpartum visits, and the pediatrician visits (well-baby visits).
- ✓ Risks of untreated depression during pregnancy may include lack of follow through with prenatal care, inadequate weight gain, preterm birth, and difficulty bonding with the unborn baby.
- ✓ For mild or moderate depression, psychotherapy alone may be effective. In moderate to severe cases, treatment may include the use of antidepressant medications as well as counseling.
- ✓ Paroxetine use in pregnant women should be avoided, if possible. A fetal echocardiogram needs to be performed.
- ✓ Postpartum psychosis usually occurs within hours to days of delivery. Incidence is 1 in 1,known history 000 women overall, but 25-35% in women with a known history of bipolar disorder.
- ✓ Post-partum depression is a subset of major depressive disorder that meets the diagnostic criteria of major depressive disorder but occurs with onset during pregnancy or within 4 weeks of delivery. Suicide is the leading cause of death in the perinatal period (pregnancy and 1-year postpartum period) and accounts for about 20% of postpartum deaths.
- ✓ First-line treatment for mild-to-moderate postpartum depression is psychotherapy (cognitive or interpersonal therapy).
- ✓ The American College of Obstetricians and Gynecologist (ACOG), recommends SSRIs as first-line pharmacotherapy for women with moderate-to-severe postpartum depression.
- ✓ For women with no previous exposure to SSRIs or NRIs, sertraline and escitalopram are considered reasonable first-line agents. Highly protein-binding SSRIs such as sertraline may be used in women who are breastfeeding. SSRIs can take up to 12 weeks to provide relief. If there is any doubt about infant exposure TMS may be an alternative.

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Information for Providers on Antidepressants during Pregnancy and Breastfeeding – March 2023

This chart is produced by the University of Illinois at Chicago (UIC) by Illinois DocAssist as a summary of research on antidepressants in human pregnancy and breastfeeding

Antidepressants Risks in Pregnancy

Safety Data: No randomized control trials. Safety data derived largely from cohort studies, registry data, and prescription monitoring registries. Older studies suggested more adverse outcomes as they did not control for confounders such as presence and severity of maternal depression which is associated with adverse outcomes. Newer and better designed studies demonstrate less risks than previously believed.

Safety Ratings: Transition from Pregnancy Category (A, B, C, D, X) to PLLR (Pregnancy, Lactation, and Reproductive Labeling) as categories are confusing and did not accurately or consistently communicate differences in fetal risk. PLLR provides a risk summary based on available data in animal and human studies as well as clinical considerations for prescribers.

- **Obstetric Risks**
  - Both maternal depression and perinatal antidepressant use are associated with increased risk of Preterm Labor by 3 gestational days [1–3]
  - SSRI's are associated with increased risk of postpartum hemorrhage (reported incidence of postpartum hemorrhage ranges between 4-18% for SSRI exposure versus 3-11% for non-exposure in women with depression) [4]

- **Infant Risks**
  - **Congenital malformations** [1,5–7]
    - New and well-designed studies show no associated increased risk for congenital malformations (including cleft lip or cardiac defects)
  - **Persistent Pulmonary Hypertension of the Newborn**[8,9]
    - Slightly increased risk with late gestational antidepressant exposure however absolute risk is still very small
    - Magnitude of risk of PPHN is smaller than previously believed
    - No association between antidepressant exposure and severe PPHN (requiring respiratory intervention)
  - **Neonatal Adaptation** [10,11]
    - Risk of transient adaptation symptoms after delivery. Non-specific criteria so rates vary widely between studies
    - Symptoms if present are usually mild and include jitteriness, restlessness, irritability, increased muscle tone, sleep disturbance, feeding problems, and rapid breathing and spontaneously resolve
    - Discontinuing SSRIs shortly (2wks) before delivery does not appear to improve neonatal outcomes (Warburton et al 2010). Stopping Medication to decrease risks of adaptation syndrome is not recommended.
  - **Neurodevelopmental** [12–16]
    - New studies do not demonstrate an association between SSRI exposure and Autism Spectrum Disorder, Intellectual Disability or ADHD
    - Previous negative studies did not control for maternal/paternal depression which increases risk of ASD in offspring
    - Some studies suggested increased risk of motor delay in antidepressant exposed infants; however infants caught up before 24 months of age

March 23rd, 2023

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Antidepressant Risks in Breastfeeding [17–19]

Safety data: Includes limited studies examining relative infant dose, medication concentration in breastmilk, and infant plasma concentration as well as reports of adverse events

Safety rating:

- **Risks:** poor feeding, lethargy, irritability, not waking to feed, jitteriness, poor weight gain.
- Infants are exposed to much higher doses in-utero, therefore women should not be counseled to discontinue medications or not breastfeed due to low comparative exposure from breast milk; most SSRIs have undetectable serum concentrations in breastfeed infants
- Dr. Hale's Lactation Risk Categories L1-L5

  L1 SAFEST – Drug has been taken by many breastfeeding women without evidence of adverse effects in nursing infants OR controlled studies have failed to show evidence of risk.
  L2 SAFER – Drug has been studied in a limited number of breastfeeding women without evidence of adverse effects in nursing infants.
  L3 MODERATELY SAFE – Studies in breastfeeding have shown evidence for mild non-threatening adverse effects OR there are no studies in breastfeeding for a drug with possible adverse effects.
  L4 POSSIBLY HAZARDOUS – Studies have shown evidence for risk to a nursing infant, but in some circumstances the drug may be used during breastfeeding.
  L5 CONTRAINDICATED – Studies have shown significant risk to nursing infants. The drug should NOT be used during breastfeeding.

Clinical Considerations [3,20]

- No medication is risk free
- The risks of psychotropic use in pregnancy and lactation must be weighed with the risks of untreated or undertreated psychiatric illness to the mother and child
- In psychotropic naive women sertraline is the drug of choice in pregnancy and breastfeeding, followed by all other SSRIs other than paroxetine
- If a patient is pregnant and euthymic on a non-first line medication, the risk of changing medications (relapse of symptoms, multiple drug exposures in pregnancy) may outweigh the benefits for the mother-infant dyad.
- Untreated or undertreated depression is associated with preterm labor, preeclampsia, increased rates of substance use, suicide, impaired bonding and attachment with infant, postpartum depression, and risk of mental disorders in infant.
- Treatment target is remission of symptoms
- Drug metabolism in pregnancy may change due to alterations in enzymatic activity such as CYP 2D6 and 3A4 and increased creatinine clearance.[21,22] May consider supra-therapeutic doses in the context.

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SSRIs (Selective Serotonin Reuptake Inhibitors)[23]

- First line for perinatal and postpartum depression due to preferred safety data, tolerability, and efficacy
- SSRI's are amongst the most well studied medications in pregnancy
- Sertraline drug of choice in psychotropic naive women who are pregnant or breastfeeding
- Paroxetine 2nd line to other SSRI's given less favorable safety data and short half life

	Medication	Advantages	Disadvantages	Absolute Infant dose in breast milk (mg/d)	Lactation Rating *	Potential adverse effects of breastfeeding
SSRIs (Selective Serotonin Reuptake Inhibitors)	**Citalopram** (10-40mg) Increase in 10mg increments	• Few interactions with other medications		0.14	L2	
	Escitalopram (5-20 mg) Increase in 5-10 mg increments	• Few interactions with other medications • Less GI side effects than other SSRI's		0.04	L2	
	Fluoxetine (20-80 mg) Increase in 10-20mg increments	• First line for depressive symptoms in adolescents	• Higher incidence of neonatal adaptation syndrome than other SSRI's • Can be more activating than other SSRI's	0.14	L2	• Longer half-life less favorable than other SSRI's in breastfeeding
	Paroxetine (20-50mg) Increase by 10mg increments		• 2nd line to other SSRI's • Short half-life, increased risk of withdrawal with missed doses	0.03	L2	
	Sertraline (50-200 mg) Increase in 25-50 mg increments	• First choice for depression during pregnancy and breastfeeding in psychotropic naive women	• More GI side effects than other SSRI's	0.04	L2	

L1 SAFEST – Drug has been taken by many breastfeeding women without evidence of adverse effects in nursing infants OR controlled studies have failed to show evidence of risk. *
L2 SAFER – Drug has been studied in a limited number of breastfeeding women without evidence of adverse effects in nursing infants.
L3 MODERATELY SAFE – Studies in breastfeeding have shown evidence for mild non-threatening adverse effects OR there are no studies in breastfeeding for a drug with possible adverse effects.
L4 POSSIBLY HAZARDOUS – Studies have shown evidence for risk to a nursing infant, but in some circumstances the drug may be used during breastfeeding.
L5 CONTRAINDICATED – Studies have shown significant risk to nursing infants. The drug should NOT be used during breastfeeding

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SNRIs (Serotonin Norepinephrine Reuptake Inhibitors)[23,24]

- Second line to SSRI's in pregnancy and postpartum
- May be beneficial for patients with comorbid neuropathic pain
- Some studies show small increased risk of spontaneous abortion
- Rebound symptoms with missed doses
- Often require slow taper due to discontinuation symptoms (dizziness, nausea, headache, paresthesia, fatigue, vomiting, irritability, insomnia, diarrhea, anxiety, hyperhidrosis)

	Medication	Advantages	Disadvantages	Absolute Infant dose in breast milk (mg/d)	Lactation Rating*	Potential adverse effects of breastfeeding
SNRIs (Serotonin Norepinephrine Reuptake Inhibitors)	**Desvenlefaxine**[27] (50mg)	• Also treats neuropathic pain • Absolute infant dose in breastfeeding half that of venlafaxine	• Least studied of the SNRI's	.016	L3	
	Duloxetine (60mg-120mg) Start 40mg, increase 20-30mg/day increments per week	• Also treats neuropathic pain and fibromyalgia • Can be given in two divided doses to aid tolerability	• Less studied than Venlafaxine in pregnancy • Small increased risk of miscarriage	<0.03	L3	
	Venlefaxine XL (37.5- 225 mg) increase in 37.5mg increments	• Also treats neuropathic pain at higher doses • More studied than other SNRI's in pregnancy	• Small increased risk of miscarriage • Higher rates of discontinuation symptoms than duloxetine	0.5	L2	

L1 SAFEST – Drug has been taken by many breastfeeding women without evidence of adverse effects in nursing infants OR controlled studies have failed to show evidence of risk. *
L2 SAFER – Drug has been studied in a limited number of breastfeeding women without evidence of adverse effects in nursing infants.
L3 MODERATELY SAFE – Studies in breastfeeding have shown evidence for mild non-threatening adverse effects OR there are no studies in breastfeeding for a drug with possible adverse effects.
L4 POSSIBLY HAZARDOUS – Studies have shown evidence for risk to a nursing infant, but in some circumstances the drug may be used during breastfeeding.
L5 CONTRAINDICATED – Studies have shown significant risk to nursing infants. The drug should NOT be used during breastfeeding.

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Non-SSRIs (Selective Serotonin Reuptake Inhibitors)/SNRIs (Serotonin Norepinephrine Reuptake Inhibitors)

	Medication	Advantages	Disadvantages	Absolute infant dose in breast milk (mg/d)	Lactation Rating*	Potential adverse effects of breastfeeding
Non-SSRIs/SNRIs	**Buproprion**[25] **Buproprion Registry** **XL** (150-450 mg) Increase in 150mg increments	• Fewer sexual side effects than SSRI's or SNRI's • Less risk of weight gain • Aids smoking cessation • Does not appear to be associated with increased risk of congenital malformations in limited studies	• Not recommended in those with eating disorders or seizure disorders • Decreases seizure threshold • May sometimes worsen anxiety	0.20	L3	• Sleep disturbance of infants reported • Isolated case reports of infant seizure
	Mirtazapine[26] (15-45mg) Increase in 15 mg increments	• Aids with sleep and promotes appetite	• Sedating • Less studied than SSRIs	0.04	L3	
	Nortriptyline (100-150 mg daily) Start 25mg daily increase in 25mg increments	• Can also be used for migraine prophylaxis	• Maternal side effects additive to pregnancy effects (sedation, constipation, tachycardia) • Orthostatic hypotension, risking decreased placental perfusion • Fetal and neonatal side effects: tachycardia, urinary retention	0.07	L2	• Dry mouth, constipation, urinary retention

L1 SAFEST – Drug has been taken by many breastfeeding women without evidence of adverse effects in nursing infants OR controlled studies have failed to show evidence of risk. *
L2 SAFER – Drug has been studied in a limited number of breastfeeding women without evidence of adverse effects in nursing infants.
L3 MODERATELY SAFE – Studies in breastfeeding have shown evidence for mild non-threatening adverse effects OR there are no studies in breastfeeding for a drug with possible adverse effects.
L4 POSSIBLY HAZARDOUS – Studies have shown evidence for risk to a nursing infant, but in some circumstances the drug may be used during breastfeeding.
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Two new treatment options:

1. In 2019 the FDA approved brexanolone (Zurlesso), an intravenous injection, the first treatment specifically for postpartum depression. Brexanolone is fast acting (improvement in 2.5 days) but requires patients to be hospitalized for a 60 hour - long infusion, during which they must be monitored for excessive sedation and loss of consciousness. Additionally, its cost before discounts and insurance is $ 34,000 per treatment.

2. 2. In August 2023, the FDA approve zuranolone (Zurzuvae), an oral pill formulation that is far more convenient to take. Zuranolone is a neuroactive steroid that is a positive modulator of the GABAa receptor. However, it will carry a boxed warning not to drive a motor vehicle or engage in potentially hazardous behavior. Costs before discounts and insurance are $ 15,900 for two weeks of treatment or $1,135 per pill. There are symptoms of withdrawal after stopping the drug, that include insomnia, palpitations, decreased appetite, hyperhidrosis, and paranoia.

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Edinburgh Postnatal Depression Scale[1] (EPDS)

Name: _____ Address: _____

Your Date of Birth: _____ _____

Baby's Date of Birth: _____ Phone: _____

As you are pregnant or have recently had a baby, we would like to know how you are feeling. Please check the answer that comes closest to how you have felt **IN THE PAST 7 DAYS**, not just how you feel today.

Here is an example, already completed.

I have felt happy:

- ☐ Yes, all the time
- ☒ Yes, most of the time
- ☐ No, not very often
- ☐ No, not at all

this would mean: "I have felt happy most of the time" during the past week. Please complete the other questions in the same way.

In the past 7 days:

1. I have been able to laugh and see the funny side of things
   - ☐ As much as I always could
   - ☐ Not quite so much now
   - ☐ Definitely not so much now
   - ☐ Not at all

2. I have looked forward with enjoyment to things
   - ☐ As much as I ever did
   - ☐ Rather less than I used to
   - ☐ Definitely less than I used to
   - ☐ Hardly at all

*3. I have blamed myself unnecessarily when things went wrong
   - ☐ Yes, most of the time
   - ☐ Yes, some of the time
   - ☐ Not very often
   - ☐ No, never

4. I have been anxious or worried for no good reason
   - ☐ No, not at all
   - ☐ Hardly ever
   - ☐ Yes, sometimes
   - ☐ Yes, very often

5. I have felt scared or panicky for no very good reason
   - ☐ Yes, quite a lot
   - ☐ Yes, sometimes
   - ☐ No, not much
   - ☐ No, not at all

*6. Things have been getting on top of me
   - ☐ Yes, most of the time I haven't been able to cope at all
   - ☐ Yes, sometimes I haven't been coping as well as usual
   - ☐ No, most of the time I have coped quite well
   - ☐ No, I have been coping as well as ever

*7. I have been so unhappy that I have had difficulty sleeping
   - ☐ Yes, most of the time
   - ☐ Yes, sometimes
   - ☐ Not very often
   - ☐ No, not at all

*8. I have felt sad or miserable
   - ☐ Yes, most of the time
   - ☐ Yes, quite often
   - ☐ Not very often
   - ☐ No, not at all

*9. I have been so unhappy that I have been crying
   - ☐ Yes, most of the time
   - ☐ Yes, quite often
   - ☐ Only occasionally
   - ☐ No, never

*10. The thought of harming myself has occurred to me
   - ☐ Yes, quite often
   - ☐ Sometimes
   - ☐ Hardly ever
   - ☐ Never

Administered/Reviewed by _____ Date _____

[1]Source: Cox, J.L., Holden, J.M., and Sagovsky, R. 1987. Detection of postnatal depression: Development of the 10-item Edinburgh Postnatal Depression Scale. *British Journal of Psychiatry* 150:782-786.

[2]Source: K. L. Wisner, B. L. Parry, C. M. Piontek, Postpartum Depression N Engl J Med vol. 347, No 3, July 18, 2002, 194-199.

Instructions for Using the Edinburgh Postnatal Depression Scale[1] (EPDS)

The 10-question Edinburgh Postnatal Depression Scale (EPDS) is a valuable and efficient way of identifying patients at risk for perinatal depression.

It is a proven screening tool.

It is easy to administer.

It can be completed at home and brought to a physician's office (OB, Pediatric, Family Practice) or the office of a mental health practitioner.

It can also be downloaded in the medical setting.

The scale indicates how the woman has felt ***during the previous week***.

It may be useful to repeat the screen in 2 weeks in questionable cases.

The EPDS score should inform but not override clinical judgment as a complete and thoughtful clinical assessment should be carried out to confirm the diagnosis.

Instructions for using the Edinburgh Postnatal Depression Scale:

1. Ask the woman to check the response that comes closest to how she has been feeling in the previous 7 days.
2. All items must be completed.
3. The mother should complete the scale herself, unless she has limited English or has difficulty with reading. She should not discuss her answers with others.

SCORING

A score of greaterthan 13 as a threshold value is:

100% sensitive, 95.5% specific for PPD[2]

Possible Depression: 10 or greater

Always look at item #10 for suicidal thoughts.

Responses are scored 0, 1, 2, or 3 according to increased severity of symptom. Items marked with an asterisk (*) are reverse scored (i.e., 3, 2, 1, and 0). The total score is determined by adding together the scores for each of the 10 items.

Good clinical care also involves asking if the mother has fears about hurting the baby or fears of the baby coming to harm.

[1]Cox, J.L., Holden, J.M., and Sagovsky, R. 1987. Detection of postnatal depression: Development of the 10-item Edinburgh Postnatal Depression Scale. *British Journal of Psychiatry* 150:782-786.

[2]Boyce, P. Stubbs, J., and Todd, A. 1987. The EPDS: validation for an Australian sample. Aust N Z J Psychiatry 27:472-6.

ACOG
The American College of Obstetricians and Gynecologists

CLINICAL PRACTICE GUIDELINE

NUMBER 4
JUNE 2023
REPLACES COMMITTEE OPINION 757, NOVEMBER 2018

Screening and Diagnosis of Mental Health Conditions During Pregnancy and Postpartum

Epidemiology

- Depression, anxiety disorders, and bipolar disorder, affect more than one in five perinatal individuals and are among the most common complications of pregnancy and the year after childbirth.
- Adolescents, military veterans, and those marginalized by racism and socioeconomic disadvantage, are at higher risk for perinatal mental health conditions and have consistently higher rates.
- Over the past decade, the prevalence of perinatal mental health conditions has increased substantially across the United States
- Perinatal depression affects approximately one in seven women (14%)
    - In 27% onset occurs before pregnancy
    - In 33% onset occurs during pregnancy
    - In 40% onset occurs postpartum

Evidence-Based Screening and Diagnostic Approaches to Perinatal Depression and Anxiety Disorders

- Everyone receiving well-woman, pre-pregnancy, prenatal, and postpartum care should be screened for depression and anxiety using standardized, validated instruments.
- Screening for perinatal depression and anxiety should occur at the initial prenatal visit, later in pregnancy, and at postpartum visits.
- Mental health screening should be implemented with systems in place to ensure timely access to assessment and diagnosis, effective treatment, and appropriate monitoring and follow-up based on severity.

Table 1. Mental Health Conditions and Associated Diagnostic Criteria*

Major Depressive Disorder

A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure

Note: Do not include symptoms that are clearly attributable to another medical condition

1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (eg, feels sad, empty, hopeless) or observation made by others (eg, appears tearful). (Note: In children and adolescents, can be irritable mood)
2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation)
3. Significant weight loss when not dieting or weight gain (eg, a change of more than 5% of body weigh in a month), or decrease or increase in appetite nearly every day. (Note: In children, consider failure to make expected weight gain)
4. Insomnia or hypersomnia nearly every day
5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down)
6. Fatigue or loss of energy nearly every day
7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick)
8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others)
9. Recurrent thoughts of death (not just fear of dying); recurrent suicidal ideation without a specific plan; a specific suicide plan; or a suicide attempt

B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning

C. The episode is not attributable to the physiological effects of a substance or another medical condition

Note: Criteria A-C represent a major depressive episode

Note: Responses to a significant loss (eg, bereavement, financial ruin, losses from a natural disaster, a serious medical illness or disability) may include the feelings of intense sadness, rumination about the loss, insomnia, poor appetite, and weight loss noted in Criterion A, which may resemble a depressive episode. Although such symptoms may be understandable or considered appropriate to the loss, the presence of a major depressive episode in addition to the normal response to a significant loss should also be carefully considered. This decision inevitably requires the exercise of clinical judgement based on the individual's history and the cultural norms for the expression of distress in the context of loss.

D. At least one major depressive episode is not better explained by schizoaffective disorder and is not superimposed on schizophrenia, schizophreniform disorder, delusional disorder, or other specified or unspecified schizophrenia spectrum and other psychotic disorders

E. There has never been a manic episode or a hypomanic episode

Note: This exclusion does not apply if all of the manic-like or hypomanic-like episodes are substance-induced or are attributable to the physiological effects of another medical condition

Table 2. Commonly Used Perinatal Mental Health Validated Screening Instruments

PMH Condition	Screening Instrument	No. of Items/Self-Administered (Y/N)	Sensitivity and Specificity	Score for Positive Screen
Depression	EPDS	10/Y	Sensitivity: 55–98% Specificity: 68–97%	≥10
	PHQ-9	9/Y	Sensitivity: 53–77% Specificity: 85–94%	≥10
Anxiety	GAD-7	7/Y	Sensitivity: 73% Specificity: 67%	≥5
	EPDS—anxiety subscale (items 3, 4, 5)	3/Y	Not enough data to estimate; correlates with GAD-7	≥5
	STAI	20/Y	Sensitivity: 81% Specificity: 78%	≥40
Bipolar disorder	MDQ	3 (Q1 with 13 items)/Y	Sensitivity: 44–90% Specificity: 61–92%	≥7 of the 13 items in Q1
	CIDI	2–3 (branching logic)/N	Sensitivity: 69–100% Specificity: 98–99%	Yes to Q3 (Q3 is asked if Q1 or Q2 are affirmed)

Abbreviations: CIDI, Composite International Diagnostic Interview; EPDS, Edinburgh Postnatal Depression Scale; GAD-7, Generalized Anxiety Scale-7; MDQ, Mood Disorder Questionnaire; PMH, perinatal mental health; PHQ-9, Patient Health Questionnaire-9; Q, question; STAI, State-Trait Anxiety Inventory.

Data from Byatt N, Masters GA, Bergman AL, Moore Simas TA. Screening for mental health and substance use disorders in obstetric settings. Curr Psychiatry Rep 2020;22:62 *and* Byatt N, Mittal LP, Brenckle L, Logan DG, Masters GA, Bergman A, et al. Lifeline for moms perinatal mental health toolkit. University of Massachusetts Medical School; 2019. Accessed December 7, 2022. https://www.umassmed.edu/lifeline4moms/products-resources/toolkits-and-apps/2019/11/lifeline4moms-perinatal-mental-health-toolkit/

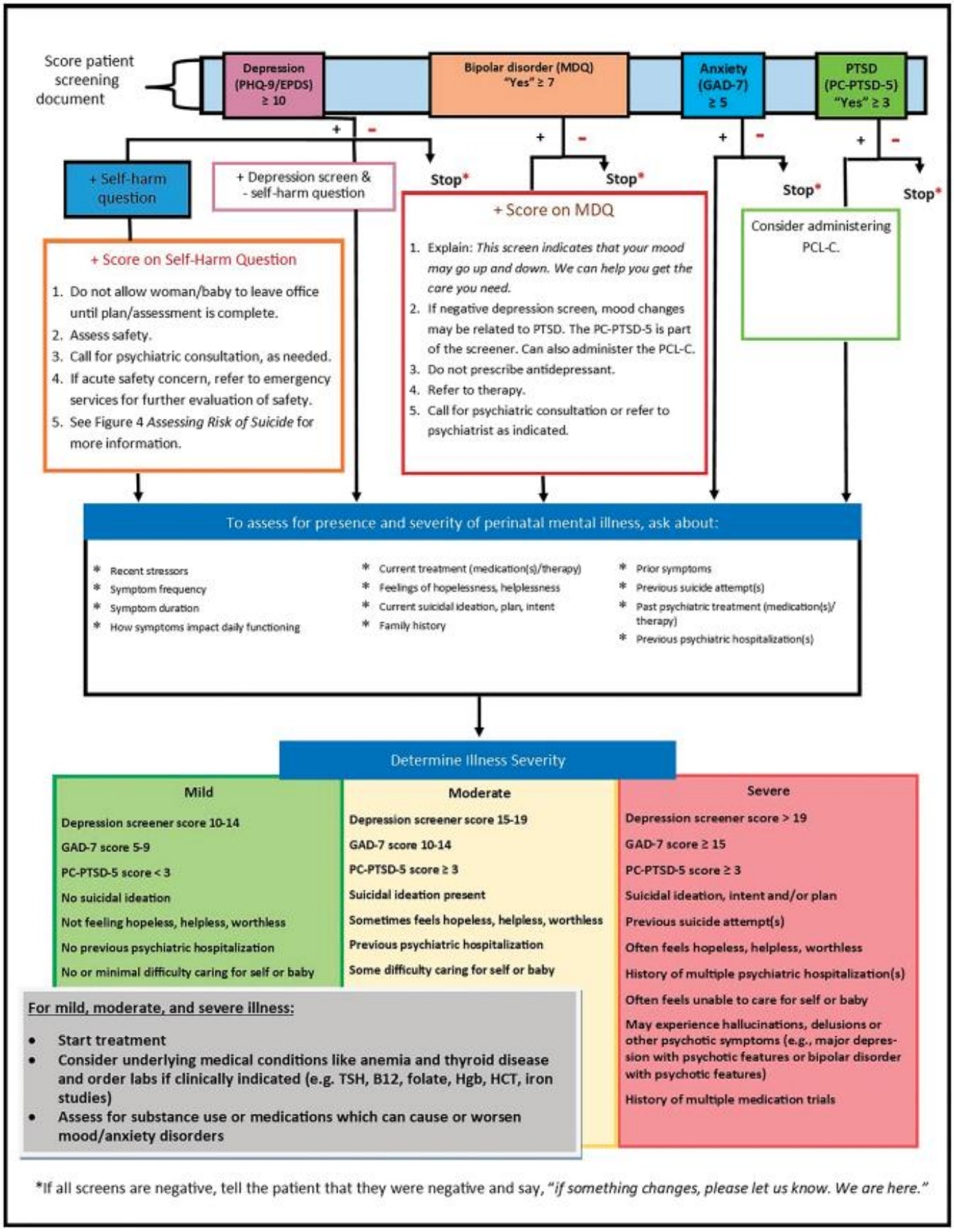

Fig. 2. Assessing perinatal mental health

PATIENT SAFETY SCREENER

This screener should be administered by the obstetric care clinician. For additional information on assessment and intervention, see Figure 4. Assessing Risk of Suicide.

**A patient presenting with a current suicide attempt is an automatic Yes on Items 2, 3, 4, 5, and 6.*

A. DETECTION (PRIMARY SCREENING)

Ask the following questions exactly as worded. If collateral information indicates ideation or attempt, document a "yes".

1. In the past two weeks, have you felt down, depressed, or hopeless? *(Not necessary to ask if PHQ9 was already administered – score it based on PHQ9 Item 2 response. 0=No, >0=Yes)*

☐ Yes ☐ No ☐ Patient unable to complete ☐ Patient refused

2. In the past two weeks, have you had thoughts of killing yourself? *

☐ Yes ☐ No ☐ Patient unable to complete ☐ Patient refused

3. In your lifetime, have you ever attempted to kill yourself? *

☐ Yes ☐ No ☐ Patient unable to complete ☐ Patient refused

3a. If yes, when did this happen?

☐ Within past 24 hours (including today) ☐ Within last month (but not today) ☐ Between 1 and 6 months ago

☐ More than 6 months ago ☐ Patient unable to complete ☐ Patient refused

B. DETECTION RESULT

"Yes" to Item 2 (ideation) OR "Within past 24 hours", "Within last month" or "Between 1 and 6 months ago" to Item 3a = ☐ Positive screen -> Proceed to C. Stratification

C. STRATIFICATION (SECONDARY SCREENING)

Assess the following six indicators using all data available to you, including patient self-report, collateral information, medical record review, and current observations.

	Yes	No	Unable to complete
4. Did the patient screen positive on BOTH active ideation AND a past suicide a past suicide attempt	1	0	
5. Has the individual begun a suicide plan? *"Have you been thinking about how you might kill yourself?"*	1	0	
6. Has the individual recently had intent to act on his/her ideation? *Do you think you might act on your thoughts?*	1	0	
7. Has the patient ever had a psychiatric hospitalization? *Have you ever been hospitalized for a mental health or substance abuse problem?*	1	0	
8. Does the patient have a pattern of excessive substance use? *Has drinking or drug abuse ever been a problem for you?*	1	0	
9. Is the patient irritable, agitated, or aggressive? *Note: This is an observation*	1	0	
Sum score (1 for each "Yes") **Total:**			

Risk level based on **highest** level category endorsed: ☐ **Mild** ☐ **Moderate** ☐ **High**

D. STRATIFICATION RESULT

	Mild risk	Moderate risk	High risk
Score from Section C	☐ 0 – 2	☐ 3 – 4	☐ 5 – 6
Critical items		☐ Suicide plan **or** intent (not both)	☐ Suicide plan **and** intent
			☐ Current attempt

Fig. 3. Patient safety screener.

Box 2. Emergent Psychiatric Evaluation

Emergent psychiatric evaluation is warranted for those:

- With suicidal ideation with an intent and plan.
- Who are unable to state reasons why they would not proceed with a suicide attempt.

In patients for whom emergent consultation is warranted, pharmacotherapy and emergent care should be obtained as soon as possible and maintained until further psychiatric assessment is completed.

ACOG
The American College of Obstetricians and Gynecologists

CLINICAL PRACTICE GUIDELINE

NUMBER 5
JUNE 2023
REPLACES PRACTICE BULLETIN NUMBER 92, APRIL 2008

Treatment and Management of Mental Health Conditions During Pregnancy and Postpartum

Safety and Efficacy of Pharmacologic Interventions for Perinatal Depressive Disorders

- ACOG recommends against withholding or discontinuing medications for mental health conditions due to pregnancy or lactation status alone.
- …recommends that psychotherapy be considered a first-line treatment for mild-to-moderate perinatal depression
- …recommends that selective serotonin reuptake inhibitors be used as first-line pharmacotherapy for perinatal depression. Serotonin-norepinephrine reuptake inhibitors are reasonable alternatives. Pharmacotherapy should be individualized based on prior response to therapy (if applicable). If there is no pharmacotherapy history, sertraline or escitalopram are reasonable first-line medications.
- The American College of Obstetricians & Gynecologists recommends consideration of zuranolone in the postpartum period (ie, within 12 months of delivery) for severe depression that has onset in the third trimester or within 4 weeks postpartum. The decision to use zuranolone should balance the benefits (ie, significantly improved and rapid symptom resolution compared with placebo) alongside challenges specific to initiating and managing this medication.
    - ACOG recommended consideration of brexanolone administration by intravenous infusion in the postpartum period for moderate-to-severe perinatal depression with onset in the third trimester or within 4 weeks postpartum. However, brexanolone is no longer commercially available in the United States as of January 1, 2025. The FDA approval was withdrawn as of April 14, 2025

Table 1. General Approach to Risk Counseling for Depression Psychopharmacotherapy	
Risks of under-treatment or no treatment for depression during pregnancy include…	**Risks of antidepressant use during pregnancy include…***
Limited engagement in medical care and self-care	PPHN
Substance use	Transient neonatal adaptation syndrome
Preterm birth	Preeclampsia (SNRIs)
Low birth weight	Spontaneous abortion (SNRIs)
Preeclampsia	
Postpartum depression	
Impaired infant attachment (which carries long-term developmental effects)	
Disrupted relationship with partner	
Suicide†	

PPHN, persistent pulmonary hypertension of the newborn; SNRI, serotonin-norepinephrine reuptake inhibitor.

*Data derived from literature that accounts for the underlying indication for antidepressant use.

†Suicide is a leading preventable contributor to maternal mortality in the United States, exceeding hemorrhage and hypertensive disorders.

Data from Trost SL, Beauregard J, Nijie F. Pregnancy-related deaths: data from maternal mortality review committees in 36 US states, 2017–2019. Centers for Disease Control and Prevention; 2022. Accessed December 7, 2022. https://www.cdc.gov/reproductivehealth/maternal-mortality/erase-mm/data-mmrc.html *and* Viswanathan M, Middleton JC, Stuebe A, Berkman N, Goulding AN, McLaurin-Jiang S, et al. Maternal, fetal, and child outcomes of mental health treatments in women: a systematic review of perinatal pharmacologic interventions. Comparative Effectiveness Review, No. 236. Agency for Healthcare Research and Quality; 2021. Accessed February 8, 2023. https://www.ncbi.nlm.nih.gov/books/NBK570101/

Pharmacological Treatment Options for Depression, Anxiety, and PTSD

- Choose antidepressant that has worked before. If antidepressant naïve, choose antidepressant based on table below with patient preference in consideration. Antidepressants are similar in efficacy and side effect profile.
- In late pregnancy, you may need to increase the dose above usual therapeutic range (e.g., sertraline 250mg rather than 50-200mg).
- If a patient presents with pre-existing mood and/or anxiety disorder and is doing well on an antidepressant, do not switch it during pregnancy or lactation. If patient is not doing well, see Figure 2: *Follow-Up Treatment of Perinatal Mental Health Conditions*.
- Evidence does not support tapering antidepressants in the third trimester.
- Minimize exposure to both illness and medication.
  - Untreated/inadequately treated illness is an exposure
  - Use lowest effective doses
  - Minimize switching of medications
  - Monotherapy preferred, when possible

First-line Treatment Options for Mild, Moderate, or Severe Depression, Anxiety Disorder, and PTSD

Medication	sertraline*	fluoxetine	citalopram**	escitalopram**
Starting dose and timing	25 mg qAM (if sedating, change to qHS)	10 mg qAM	10 mg qAM	5 mg qAM
Initial increase after 4 days	↑ to 50 mg	↑ to 20 mg	↑ to 20 mg	↑ to 10 mg
Second increase after 7 more days	↑ to 100 mg			
Reassess Monthly (increase as needed until symptoms remit)	↑ by 50 mg	↑ by 20 mg	↑ by 10 mg	↑ by 10 mg
Therapeutic range***	50-200 mg	20-80 mg	20-40 mg	10-20 mg
Individualized approach to titration	Slower titration (e.g., every 10-14-days) is often needed for patients who are antidepressant naïve or with anxiety symptoms			

*Lowest degree of passage into breast milk compared to other first-line antidepressants; **Side effects include QTc prolongation (see below);
***May need higher dose in 3rd trimester and when treating an anxiety disorder
In general, if an antidepressant has helped during pregnancy, it is best to continue it during lactation.
Prescribe a maximum of two (2) antidepressants at the same time.

Second-line Treatment Options for Mild, Moderate, or Severe Depression, Anxiety Disorder, and PTSD

Medication	duloxetine 30 mg ***	venlafaxine 37.5 mg	fluvoxamine 25 mg	paroxetine 10 mg***	mirtazapine 7.5 mg	bupropion HCL 150 mg
Starting dose and timing	qAM	qAM	qHS	qAM (if sedating, change to qHS)	qHS	qAM
Initial increase after 4 days	↑ to 60 mg	↑ to 75 mg	↑ to 50 mg	↑ to 20 mg	↑ to 15 mg	
Second increase after 7 more days			↑ to 100 mg			
Reassess Monthly (increase as needed until symptoms remit)	↑ by 30 mg	↑ by 75 mg	↑ by 50 mg	↑ by 10 mg	↑ by 15 mg	↑ by 150 mg
Therapeutic range ***	30-120 mg	75-300 mg	50-200 mg	20-60 mg	15-45 mg	300-450 mg
Individualized approach to titration	Slower titration (e.g., every 10-14-days) is often needed for patients who are antidepressant naïve or with anxiety symptoms					

***May need higher dose in 3rd trimester and when treating an anxiety disorder

	Temporary (days to weeks)	Long-term (weeks to months)
General side effects oral antidepressants	Nausea (most common)	Increased appetite/weight gain
	Constipation/diarrhea	Sexual side effects
	Lightheadedness	Vivid dreams/insomnia
	Headaches	**QTc prolongation (citalopram & escitalopram)

- Tell women to take medication with food and only increase dose if tolerating; otherwise wait until side effects dissipate before increasing.
- Start medication in morning; if patient finds it sedating recommend that she takes it at bedtime

Medication Treatment for Moderate/Severe Depression with Onset in Late Pregnancy or Within 4 weeks postpartum – Brexanolone

Brexanolone is an FDA-approved medication that can be considered for treatment of moderate to severe postpartum depression.

Brexanolone:
- is a formulation of intravenous allopregnanolone (a neurosteroid) that acts on GABA-A receptors
- requires an IV infusion over 60 hours
- has a faster onset of action (symptom reduction in 1-2 days) compared to available oral antidepressants, which generally take 4-8 weeks to work
- has been shown to maintain the reduction in depression symptoms at 30 days post-infusion

When is Brexanolone indicated?

If onset of depression occurs in 3rd trimester through 4 weeks postpartum and if patient is <6 months postpartum at screening, consider Brexanolone (IV allopregnanolone infusion over 60 hours in an inpatient setting).

More information can be found at Reprotox and LactMed on all pharmacological treatments

Fig. 1. Starting treatment for perinatal mental health conditions. FDA, U.S. Food and Drug Administration; GABA-A, gamma aminobutyric acid type A; IV, intravenous; mg, milligrams; PTSD, posttraumatic stress disorder; qAM, every morning; qHS, every bedtime.
Modified from Byatt N, Mittal LP, Brenckle L, Logan DG, Masters GA, Bergman A, et al. Lifeline for Moms Perinatal Mental Health Toolkit. University of Massachusetts Medical School; 2019. Accessed March 20, 2023. https://www.umassmed.edu/lifeline4moms/products-resources/toolkits-and-apps/2019/11/lifeline4moms-perinatal-mental-health-toolkit/

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Yonkers, Kimberly A., MD, et al. *The Management of Depression during Pregnancy: A Report from the American Psychiatric Association and the American College of Obstetricians and Gynecologists.* General Hospital Psychiatry 31 (2000) 403-413.

Suicide and maternal mortality. Chin K et al Curr Psychiatry Rep. 2022; 24(4) 239-275

Concerns That May Limit the Use of Zuranolone. Prasad V, Allely D JAMA Vol 331,No 2 January 9, 2024

A Fast-Acting Pill received Approval for Postpartum Depression-Is It a Game Changer? Rubin R JAMA Network August 23, 2023

Resources

American Psychological Association. Brochure: *Postpartum Depression* May be downloaded from https://www.apa.org/pVwomen/resources/reports/postpartum-depression-brochure-2007.pdf

The American College of Obstetricians and Gynecologists http://www.acog.org

The American College of Obstetricians and Gynecologists. *Postpartum Depression.* Patient educational Pamphlet AP0 91. Washington, DC:American College of Obstetricians and Gynecologists; 2013.
Print copies can be ordered online at http://sales.acog.org or by calling 1-800-762-2264.

Massachusetts General Hospital Center for Women's Health: Reproductive Psychiatry Resource and Information Center. Psychiatric Disorders During Pregnancy
http://www.womensmentalhealth.org/specialty-clinics/psychiatric-disorders-during-pregnancy

Massachusetts Child Psychiatry Access Project (MCPAP) for Moms Toolkit available at https://www.mcpapformoms.org/Toolkits/Toolkit.aspx

Postpartum Support International, 6706 SW 54th Avenue, Portland, OR 97219. (503) 894-9453. Available at http://www.postpartum.net Support Helpline: 1-800-9444PPD (4773)

The 2020 Mom Project website: http://www.2020mom.org/

US Department of Health and Human Services; Health Resources & Services Administration, 2010. *Depression during and After Pregnoncy: A Resource for Women, Their Famiies, and Friends.* Patient educational brochure. Available online at www.mchb.hrsa.gov/pregnancyandbewnd/depression
Print copies can be obtained from the HRSA Information Center 1-888-Ask-HRSA.

Postpartum Support International (PSI) website: https://www.postpartum.net/professionals/screening/